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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,282	12/20/2001	Paul Young	PZ007G62AP1D1	4789

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,282	YOUNG ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/29/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 16, 37, 53-54 and 75 have been amended.

Claims 76-85 have been added.

2. Claims 1-85 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

5. The objections to the specification for various formal matters, parts a-c, are withdrawn in view of Applicant's arguments and amendments to the specification.

6. The objection to claim 54 (part d) for missing the term "of" is withdrawn in view of the amendment to the claim filed 9/29/2004.

7. The rejections of claims 6, 16 and 37-75, parts a-c, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of Applicant's arguments and amendments to the claims.

8. The rejection of claims 7, 29, 44 and 67 under 35 U.S.C. 112, first paragraph, enablement (part b) because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with the claims is withdrawn in view of Applicant's arguments.

9. The rejection of claims 38-75 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with the claims is withdrawn in view of Applicant's successful completion of the deposit requirements.

Response to Arguments

10. The rejection of claims 1-75 and newly added claims 76-85 under 35 U.S.C. 101 because the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility is maintained.

The response filed 9/29/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that the specification at page 99 teaches that "the protein product of this gene is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia" where an insufficient number of hematopoietic cells contributes to the diseases and where bone marrow transplantation and/or reconstitution can be used to treat such diseases and "this gene may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages and in the differentiation and/or proliferation of various cell types." Further, Applicant cites post-filing date publications (Lui et al, WO 00/56889, WO 02/00690 and Makino et al), to further corroborate the specific and substantial utilities asserted in the specification. In response to these arguments, the instant specification as filed does not

support the asserted utilities. The asserted utilities at pages 98-99 for Gene no. 62, which encodes the polypeptide of SEQ ID NO:310 are not substantial utilities. The data set forth in the specification is preliminary at best. The specification as filed does not teach whether the polypeptide of SEQ ID NO:310 is either overexpressed or underexpressed in a particular disease, nor does the specification disclose any activity for SEQ ID NO:310, nor does the specification teach that SEQ ID NO:310 share significant homology to any known protein, nor does the specification disclose what physiological significance SEQ ID NO:310 plays. Thus, SEQ ID NO:310 is a totally new, uncharacterized polypeptide with no well-established utility. In fact, Lui et al, which was published two years after the filing date of the instant application and cited by applicant in support of the asserted utilities in the specification, hypothesizes that C17 [identical to SEQ ID NO:310] may function as a cytokine (see page 291, right column). Lui et al continues, "we are now investigating the biological functions of C17. One possibility is that C17 functions as an autocrine/paracrine cytokine to act on CD34+ cells. Alternatively or additionally, C17 may act on the surrounding cells such as marrow stromal cells that lack C17 gene expression." (see page 291, right column). Further, Lui et al state "we have not yet found any existing molecule that shows significant homology to the amino acid sequence of the C17 gene in public databases." (see page 291, right column). Therefore, in the words of Lui et al published two years after the effective filing date of the instant application the polypeptide of SEQ ID NO:310 (C17) is of unknown biological function and additional experimentation is required to determine what biological function this polypeptide has. Thus, in view of the lack of any

experimental data in the specification as filed and as evidenced in the teachings of the post-filing publication of Lui et al, the asserted utilities in the specification are not supported by a substantial utility or a well-established utility.

Thus, the proposed uses of the polypeptide of SEQ ID NO:310 and, in turn, an antibody that binds to this polypeptide as useful in proliferation and differentiation, particularly of hematopoietic stem cells, are simply starting points for further research and investigation into potential practical uses of the polypeptide and antibody that binds thereto. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[I]t is not a reward for the search, but compensation for its successful conclusion."

11. Claims 1-75 and newly added claims 76-85 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention is maintained.

12. The rejection of claims 1-75 and newly added claims 76-85 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims is maintained.

The response filed 9/29/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that as of the claimed priority date of the instant application, methods of making and using a diverse array of antibody types were routine for those of ordinary skill in the art and the specification teaches various types of antibodies that may be produced against the protein of SEQ ID NO:310 and assays that may be used, such as radioimmunoassays, competitive-binding assays, Western blot analysis, ELISA assays and describes how antibodies may be used to carry out in vivo imaging. In response to this argument, the examiner agrees that methods of making and using a diverse array of antibody types were routine for those of ordinary skill in the art and one of ordinary skill in the art would know how to use antibodies that bind the polypeptide of SEQ ID NO:310 in the assays disclosed in the instant specification, however, this was not the point of the instant rejection. The issue with respect to the instant rejection is that one of ordinary skill in the art would not know how to use the instantly claimed antibodies that bind the polypeptide of SEQ ID NO:310 because the instant specification does not disclose a nexus between the expression of SEQ ID NO:310 with any particular disease state or condition and the specification does not teach or predict whether SEQ ID NO:310 would be overexpressed or underexpressed in a particular disease state such that an antibody, which specifically binds SEQ ID NO:310 could be predictably used for diagnosis or immunotherapy. The specification does not disclose whether an antibody specific for SEQ ID NO:310 would be an agonist

or an antagonist in any particular disease state or condition. The enablement in this case relies on the limited disclosure that the gene encoding the polypeptide of SEQ ID NO:310 is expressed in fetal liver and fetal spleen, however, the claims are drawn to an antibody that binds the polypeptide encoded by gene no. 62. The specification does not support a nexus between a disease state or condition and the expression of SEQ ID NO:310 and thus, represents an invitation to one of ordinary skill in the art to experiment to determine such a nexus and therefore, experimentation into the practical uses for an antibody to SEQ ID NO:310. With respect to the lack of a necessary correlation between gene expression and protein expression, applicant argues that although it is true that mRNA expression levels do not always exhibit a direct proportional correlation with protein expression levels, the lack of at least some general connection is the exception rather than the norm and applicant argues that the art of Fu et al, Powell et al, Lewin et al and Jang et al were in fact, worthy of publication precisely because they represent exceptions to the norm, not because they are paradigms of the norm. In response to this argument, Applicant has not provided any objective evidence that it is the norm that mRNA levels exhibit a direct proportional correlation with protein expression levels. Further, irrespective of the reasons for their publication, the references cited by the examiner (Fu et al, Powell et al, Lewin et al and Jang et al) evidence that it cannot be said with any certainty that there is always such a direct proportional correlation between mRNA expression levels and protein expression levels. The response also argues that Alberts et al in contrast to the references cited by the examiner teaches "For most genes transcriptional controls are paramount. This makes

sense because of all the possible control points...only transcriptional control ensures that no superfluous intermediates are synthesized." The response states that one of ordinary skill in the art most often looks to mRNA expression levels as predictive of the relative protein expression levels and as corroborated by Alberts et al most genes are, in fact, transcribed into mRNA and translated into protein in direct proportion to their relative mRNA expression levels. In response to these arguments, Alberts et al (Molecular Biology of the Cell, 3rd edition, 1994, page 465) illustrate post-transcriptional regulation of ferritin wherein the translation of ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferring receptor mRNA is degraded and no transferin receptor polypeptide is translated. Further, as evidenced by Gokman-Polar et al (Cancer Research, 2001, 61:1375-1381), the absence of any necessary correlation between increased mRNA levels and increased protein levels is made explicit by Gokman-Polar et al who teaches "Quantitative reverse transcription-PCR analysis revealed that PKC mRNA levels do not directly correlate with PKC protein levels, indicating that PKC isoenzyme expression is likely regulated at the posttranscriptional/translational level" (see abstract). Gokman-Polar et al show in figures 6 and 7 that there is no increase in mRNA expression for any of the isoenzymes, while the protein is significantly overexpressed as shown by figures 4 and 5. Therefore, in view of the art cited by the examiner in the 112 first rejection (Fu et al, Powell et al, Lewin et al and Jang et al) and as evidenced by Gokman-Polar et al it is not necessarily the norm that gene expression, or even transcription, parallels protein expression. Thus, in view of the totality of evidence, the skilled artisan would not assume that gene

expression necessarily parallels or is predictive of protein expression, but would perform the experiment to verify it.

Accordingly, in view of applicant's limited disclosure stating that gene no. 62, which encodes the polypeptide of SEQ ID NO:310 is expressed in fetal liver and spleen and the lack of a disclosed nexus between the expression of gene no. 62 or SEQ ID NO:310 and a particular disease state or condition and the lack of a necessary correlation between gene expression and protein expression as discussed above, one of ordinary skill in the art would not know how to use the claimed antibodies in any diagnostic or immunotherapeutic setting with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed antibodies and absent working examples providing evidence which is reasonably predictive that the claimed antibodies are effective for diagnosis or immunotherapy correlated with a particular disease or condition.

New Grounds of Rejections

13. Claims 76-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 76-85 are indefinite for reciting "Secreted Protein HEMAE80 expressed on the surface of cells" in claim 76. The specification does not disclose whether the polypeptide encoded by Gene No. 62 is a secreted protein or is a transmembrane protein. The specification does not disclose any transmembrane domain of SEQ ID

NO:310, thus, it is unclear what is meant by the phrase "secreted protein expressed on the surface of cells" because a secreted proteins do not contain transmembrane domains and are not expressed on the cell surface. Lui et al (Genomics, 65:283-292, 2000, Ids reference AD, filed 5/14/04) teaches a polypeptide that is identical to SEQ ID NO:310 (C17) as a secreted protein with no transmembrane domains.

14. Claims 76-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Newly added claims 76-85 have introduced NEW MATTER into the claims. The response filed 9/29/2004 states that support for the newly added claims 76-85 can be found at table 1, page 327, row 3 as indicated as "Gene No. 62"; and page 389, lines 11-17. There is insufficient written description for an antibody that binds secreted protein HEMA80 (SEQ ID NO:310) expressed on the surface of cells in a cell culture because the instant specification does not disclose that the HEMAE80 protein is expressed on the surface of cells nor does the specification provide adequate written description for any transmembrane domain(s) of the polypeptide of SEQ ID NO:310. Therefore, applicant was not in possession of HEMAE80 expressed on the surface of cells and, in turn, an antibody that binds to HEMAE80 expressed on the surface of cells.

Applicant is required to provide support for all limitations in the claim in the specification or claims as originally filed or remove then from the claims.

Conclusions

15. No claim is allowed.

16. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827